REMARKS

By this amendment, claims 1, 5, 8, 13 and 15 are amended to more precisely recite the features of the claims. New claim 21 is added. Claims 6, 11 and 16-19 are canceled. No new matter is introduced. Support for the amendments may be found at least at page 7, lines 21-34 (claims 1, 5, 8, 15 and 21), page 11, line 3 (claim 8), and Figure 2 (claims 1, 5, 8, 15 and 21) of the specification. Claims 1-5, 7-10, 12-15, 20 and 21 are pending. Reconsideration and allowance of the claims in view of the above amendments and the remarks that follow are respectfully requested.

Claim Rejections Under 35 U.S.C. §103

In the Final Office Action mailed October 30, 2007, claims 1-6, 8-13 and 15 stand rejected under 35 U.S.C. § 103(a) over Harley et al. (hereinafter "Harley") in view of Elmore et al. (hereinafter "Elmore") for reasons stated on pages 2-10 of the Office Action. Claims 7 and 14 stand rejected under 35 U.S.C. § 103(a) over Harley in view of Elmore and further in view of Choo et al. (hereinafter "Choo") for reasons stated on pages 11-12 of the Office Action. Claim 20 stands rejected under 35 U.S.C. § 103(a) over Harley in view of Elmore and further in view of Nakamura et al. (hereinafter "Nakamura") for reasons stated on pages 12-14 of the Office Action. Applicants respectfully traverse the rejection.

Independent Claim 1, as amended, is directed to a method for detecting and quantifying telomerase activity in a biological sample, the method comprising the steps of: adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer, and nucleoside triphosphates; **a second reaction mixture comprising a second primer and a DNA polymerase**; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube; incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product having a 3' end; **elongating the extended product at the 3' end by template-independent polyadenylation or template-independent ligation;** admixing the extension product with the second reaction mixture by melting the wax layer; amplifying the elongated extension product using a real-time polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell; and quantifying the amplified extension product using a control template.

Independent claim 8, as amended, is directed to a method for detecting and quantifying telomerase activity in a sample cell, the method comprising the steps of: suspending the sample cell in a cell suspension; **passing the cell suspension through a needle 2-5 times**; introducing into a sample cell a first primer and nucleoside triphosphates; incubating the sample cell under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product having a telomeric repeat sequence at a 3' end, **adding a polyadenylate sequence to the 3' end of the extension product by tempalte-independent polyadenylation or template-independent ligation;** amplifying the polyadenylated extension product using real-time polymerase chain reaction **in the presence of a second primer that comprises a sequence complementary to a junction of the telomeric repeat sequence and thye polyadenylate sequence at the 3' end of the polyadenylated extension product**; and quantifying the amplified extension product using a control template.

Independent claim 15, as amended, is directed to a method for detecting and quantifying telomerase activity in a biological sample, the method comprising the steps of: adding the biological sample to a reaction tube comprising: a first reaction mixture comprising a first primer and nucleoside triphosphates; **a second reaction mixture comprising a second primer and a DNA polymerase**; and a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube; incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product; **elongating the extended product at a 3' end by template-independent polyadenylation**; admixing the extension product with the second reaction mixture by melting the wax layer; amplifying the extension product using a real-time polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell; and quantifying the amplified extension product using a control template, **wherein the second primer comprises a nucleotide sequence that is complementary to the nucleotide sequence at a 3' end of the elongated extension product**.

Harley generally describes a method for detecting and quantifying telomerase activity. Harley does not teach or suggest "a second reaction mixture comprising a second primer and a DNA polymerase," as recited in claims 1 and 15.

The Examiner admits that Harley does not teach a method wherein both the polymerase and second primer are separated from the first reaction mixture by a wax layer. The Examiner,

however, alleges that "the purpose of the wax barrier is to separate the telomerase extension reaction from the amplification reaction … there is no functional reason or obvious advantage to have or not have one of the reagents present in the telomerase mixture" (the Office Action, page 10).

Applicants respectfully submit that biotechnology is generally considered an unpredictable art. It is well known to one skilled in the art that the presence of additional primers in a reaction mixture may lead to unexpected results, especially in a situation where two reactions (i.e., the telomerase-mediated primer extension and PCR amplification) are carried out sequentially in the same tube. In fact, Applicants have demonstrated that the removal of the taq polymerase and/or the second primer from the telomerase-extension reaction has a significant impact on the reaction dynamics of the subsequent PCR amplification. In particular, separation of the second primer and Taq polymerase from the telomerase-extension reaction unexpectedly lead to increased specificity of the assay system (see attached Exhibit 1: Declaration from Dr. Zhuangwu Li).

Moreover, Harley does not teach or suggest the step of elongating the extended product at the 3' end by template-independent polyadenylation or template-independent ligation, as recited in claims 1, 8 and 15. Harley also fails to teach or suggest a second primer comprising a nucleotide sequence that is "complementary to a junction of the telomeric repeat sequence and thye polyadenylate sequence at the 3' end of the polyadenylated extension product," as recited in claim 8, or is "complementary to the nucleotide sequence at a 3' end of the elongated extension product," as recited in claim 15.

In addition, Harley does not teach or suggest the step of passing the cell suspension through a needle 2-5 times, as recited in claim 8. Harley mentions fine needle aspirates or biopsy of tumor tissue. One skilled in the art would understand that the purpose of a fine needle biopsy is to take out a small piece of tissue from a target organ. A needle biopsy does not involve a "cell suspension" and does not require "passing the cell suspension through a needle 2-5 times."

Elmore, Choo and Nakamura do not cure the deficiency of Harley. Elmore generally describes a method of quantitative analysis of telomerase activity in breast cancer specimens. Choo generally describes a method wherein the control template has a nucleotide sequence recited in SEQ ID NO: 2. Nakamura generally describes a method to monitor the effectiveness

of treatment of a subject with an agent that inhibits telomerase activity. Elmore, Choo and Nakamura, however, fail to teach or suggest separating the second primer and Taq polymerase from the telomaerase extension reaction, elongating the extended product at the 3' end by template-independent polyadenylation or template-independent ligation, or passing the cell suspension through a needle 2-5 times.

Therefore, Applicants respectfully submit that Harley, Elmore, Choo and Nakamura, individually or in combination, do not render claims 1, 8 and 15 obvious. Applicants further submit that claims 2-5, 7, 9, 10, 12-14 and 20 are patentable because they depend from one of claims 1, 8, and 15, and because they recite additional patentable subject matter. Withdrawal of rejection to claims 1-5, 7-10, 12-15, and 20 is respectfully requested. New claim 21 is patentable over Harley, Elmore, Choo and Nakamura for the same reasons discussed above.

Claims 6, 11, and 16-19 have been canceled. Rejection to these claims are now moot.

In view of the above amendments and remarks, Applicant respectfully submits that the application is in condition for allowance. Prompt examination and allowance are respectfully requested. Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

Date: **January 24, 2008**

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Enclosure: Exhibit 1: Declaration from Dr. Zhuangwu Li.